Allergy Abstracts

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Announcement

ALLERGY ABSTRACTS has been published since 1936 by members of the Allergy Division of the Jewish Hospital of Brooklyn. The Editorial Board is comprised of former residents of this department who contribute their services.

ALLERGY ABSTRACTS selects and abstracts those articles in the literature which may be of clinical or theoretical interest to workers in the field of allergy. Each abstract represents a summary of the author's findings and views, and its inclusion in ALLERGY ABSTRACTS does not imply approval of its contents by the editor.

—*The Editors*

Asthma and Hay Fever

The Use of Artificial Respiration in Pulmonary Emphysema Accompanied by High Carbon Dioxide Levels. Boutourline-Young, H. J., and Whittenberger, J. L.: J. Clin. Investigation **30**: 838, 1951.

Patients with advanced emphysema can be shown to have decreased respiratory center sensitivity to carbon dioxide, the principle stimulus to breathing being hypoxia. Administration of oxygen then induces apnea and may lead to a lethal accumulation of carbon dioxide. Two cases of severe emphysema were treated by the use of a body respirator for from 3 to 5 days. Blood and alveolar gas studies showed the deleterious effects of oxygen administration and the inefficacy of the addition of 5.25 per cent carbon dioxide prior

to use of the respirator. One patient evidenced dramatic improvement, was enabled to return to work, and has maintained his improvement for 12 months following this treatment. Sensitivity of respiration to carbon dioxide returned. The second patient showed improvement to normal despite constant "fighting" of the respirator but relapsed about 36 hours afterward. The theoretical basis for the treatment is discussed in detail. K.

Problems of the Geriatric and Their Clinical Management. Tuft, L.: J. A. M. A. **146**: 1480, 1951.

The rather well-established idea that asthma beginning after age 40 is practically always of the infectious or intrinsic type is questioned. Allergic bronchial asthma as well as hay fever, urticaria, and atopic dermatitis can and do begin in people past 40. Although it is true that asthma in older individuals is usually not accompanied by the marked skin sensitivity to specific allergens found in younger persons, significant positive skin tests of lesser intensity are often demonstrable. The initial attacks may be due to acquired sensitization to inhalants, foods, drugs, and bacterial allergens, or to endocrine or psychoosomatic factors. Sinus disease, unless accompanied by frank, purulent discharge, is rarely of significance in the etiology of geriatric asthma. Food sensitivity is not an uncommon cause of symptoms.

In the differential diagnosis of asthma in the geriatric patient, it is necessary to exclude the various types of cardiac and intrathoracic pathology seen in this age group. Mediastinal tumors of neoplastic, aneurysmal, or lymphatic origin may produce wheezing. Hypertensive cardiovascular disease producing a paroxysmal type of wheezing dyspnea, usually nocturnal, the so-called cardiac asthma, may occur independently of, or concomitantly with, true bronchial asthma. It is believed to be due to a sudden relative left ventricular failure in a patient whose right ventricle is functionally normal. This sudden failure produces, in turn, acute pulmonary hypertension, secondary intense pulmonary emphysema, and edema often associated with precordial pain or oppression. Such attacks may be difficult to distinguish from bronchial asthma by examination alone, but the short duration of the symptoms, the presence of hypertension, left-sided cardiac enlargement, cardiac murmurs, and electrocardiographic evidence of impairment of conductivity make the diagnosis of this somewhat uncommon condition comparatively easy. Another condition which may simulate asthma is the chronic bronchitis commonly associated with chronic emphysema in older individuals. The wheezing in such cases is usually secondary to the cough and is more or less continuous, rather than paroxysmal in nature.

The treatment of the geriatric asthmatic is essentially the same as that of the younger patient. Care must be exercised in the administration of extracts to older patients since constitutional reactions are easily induced and prolongation and aggravation of the asthma may result from overdosage. F.

Studies on the Relative Oxygen Saturation of the Blood in Spontaneous and Provoked Bronchial Asthma. Arner, B., Wiholm, S., and Oehnell, L.: Acta Allergologica **3**: 156, 1950.

Using the Berg oxymeter, oxygen saturation studies were carried out during the height of asthmatic attacks in 3 groups of patients. Group I included patients whose asthmatic attacks were experimentally provoked by inhalation of specific allergens. Group 2 consisted of patients with spontaneous acute attacks of asthma. Group 3 comprised patients with exacerbations of asthma while in a chronic asthmatic state.

The asthmatic attack, whether spontaneous or experimentally induced, was followed by hypoxia. The state of hypoxia was more pronounced in the spontaneous and induced forms of asthma than it was in those asthmatic attacks classified as exacerbations of a chronic asthma with bronchitic complications.

A varying effect of the intravenous inection of adrenalin was observed. Patients with both spontaneous and induced attacks showed a rapid, pronounced increase of their relative oxygen saturation, usually of short duration. In cases complicated by bronchitis, intravenous adrenalin had a varying effect upon the hypoxia.

As the asthmatic attack subsided, the relative oxygen saturation increased. The administration of oxygen during an attack increased the oxygen saturation to a small extent only. Both theophylline and adrenalin administration caused an immediate increase of the relative oxygen saturation with clinical improvement of the patient. H.

Denervation of the Lungs for Bronchial Asthma. Case Report. Selman, M. W.: Ann. Allergy **8**: 328, 1950.

The treatment of intrinsic bronchial asthma by denervation of the lungs is reported. The patient, a 34-year-old woman, had had asthma for 5 years. Symptoms had become progressively more severe and the patient was not relieved by any of the usual therapeutic measures nor by x-ray therapy, visits to Arizona and California, psychiatric therapy, or antiallergic treatment. Surgical denervation of the left lung was followed by improvement lasting one month. After the denervation of the right lung, the patient experienced marked relief from symptoms lasting for more than one year. Only sensitivity to potassium iodide was mentioned as an etiologic factor. E. W.

Chromatographic Analysis of Ragweed Pollen Extract. Perlman, E.: Bull. New York Acad. Med. **27**: 586, 1951.

Crude giant ragweed pollen extract was subjected to chromatographic studies. The substances eluted following the application of various reagents to the paper were studied by means of the scratch test for antigenic potency. The results showed the presence of a large number of components in the crude pollen extract. At least two of these constituents produced positive skin reactions when tested in susceptible individuals. R. W.

An Investigation of the Role of Fungi in Patients With Bronchial Asthma and Anthracosis. Piekarski, J. W.: Ann. Allergy **8**: 383, 1950.

Forty-seven miners with physical disabilities resulting from "anthracosis with manifestations of bronchial asthma-like syndrome" were tested intracutaneously with an extract of Penicillium (PAC) Zaleskii. This mold forms a coat of mycelium on the timbers deep in certain mines and its spores are found in the air of these mines. Of 20 miners tested in 1942 with extracts containing 100 and 500 protein nitrogen units per ml., 30 per cent gave slight or doubtful reactions. Most of these had been engaged in mining from 33 to 40 years. Of another group of 27 miners tested in 1948 with similar extracts, 21 per cent gave doubtful reactions when tested with this extract containing 100 protein nitrogen units per ml. Seven per cent of these 27 miners responded with one-plus reactions and 37 per cent with doubtful reactions when tested with the Penicillium extract containing 1000 units per ml. Most of these reactions appeared in miners who had been employed for more than 20 years. It was concluded that both the doubtful and the positive reactions were nonspecific in origin. E. W.

Dermatitis

Hypersensitivity to Penicillin. Sonck, C. E.: Nord. med. **43**: 779, 1950.

The writer presents an extensive review of the literature on hypersensitivity to penicillin. Urticaria was found to occur in approximately 16 per cent of patients receiving penicillin. A number of cases of bullous and exfoliative dermatitis, including several fatalities, have been reported. Dermatophytic type of eruptions occurred chiefly in patients with existing fungus infections. The incidence of contact type dermatitis reactions was definitely greater in patients with eczema or allergic diseases. Cheilitis, glossitis, stomatitis, and pharyngitis have been reported following the oral administration of penicillin. The incidence of sensitization to penicillin is approximately 10 per cent. H.

Contact Dermatitis Due to Cinnamon: Recurrence of Dermatitis Following Oral Administration of Cinnamon Oil. Leifer, W.: Arch. Dermat. & Syph. **64**: 52, 1951.

A 36-year-old woman with a chronic vesicular dermatitis of the hands of 5 years' duration developed a typical contact dermatitis of the face, the presternal region and the right forearm with an exacerbation of the lesions of the hands. She gave a history of having used a new toothpaste shortly before the onset of the rash. Patch testing was performed with the ingredients of the toothpaste. Positive reactions were obtained with 1 per cent cinnamon oil in alcohol. The eruption cleared when contact with cinnamon was avoided. Ingestion of cinnamon powder was followed by itching of the hands within 12 hours. Ingestion of cinnamon oil was followed by itching and vesiculation of the hands after 5 days (delayed reaction) on one occasion and after 12 hours on a second occasion. The lips and buccal mucous membranes were not involved. C.

Contact Dermatitis Caused by Bamboo. Schiff, B. L.: Arch. Dermat. & Syph. **64**: 66, 1951.

Three men employed in a factory that manufactured bamboo tennis rackets developed typical contact dermatitis lesions on the exposed parts shortly after handling a new shipment of bamboo from Japan. Patch tests with scrapings of the bamboo gave positive reactions in all three. These are the first cases of dermatitis due to bamboo which have been reported. C.

An Increase of Dermatitis Due to Felt of Hats. Spier, H. W., and Schutz, K. H.: Hautarzt **1**: 519, 1950.

Five cases of contact dermatitis of the forehead are reported. In all instances, patch tests performed with the hat felt gave positive reactions, while those made with the hatbands and with formalin resulted negatively. In 3 of the 5 cases, patch tests with 0.2 per cent para-chinon and 2 per cent chinhydron were positive. The writers believe that group sensitivity to the aromatic chinoid compounds is common. H.

Successful Treatment of Dermatitis Due to Chrysotherapy With Adrenocorticotropic Hormone. Steinberg, C. L., and Roodenburg, A. I.: J. A. M. A. **146**: 1225, 1951.

A 40-year-old man who had received gold therapy for rheumatoid arthritis developed a dermatitis 3 months after the discontinuation of treatment. The administration of 15 mg. of ACTH every 6 hours provided very little relief, but the erythema began to fade, when dosage was increased to 20 mg. every 6 hours. Seven days after the institution of the larger dose the rash had disappeared. F.

Activity of the Antihistamine Drugs. A Method of Assessment in Man. Ross, A.: Lancet **2**: 62, 1951.

On the supposition that erythema produced in human skin by exposure to either natural or artificial ultraviolet light is due to histamine liberation, subjects were exposed to standard graded amounts of ultraviolet radiation both before and following antihistamine therapy. Both Thephorin and Phenergan failed to alter the amount of erythema produced, while Histantin substantially reduced the amount of erythema observed in several patients. This method offers a new means for assessing, in vivo, the relative activity of antihistamine drugs. R. W.

Some Observations on the Use of Adrenocorticotropic Hormone in Atopic Dermatitis in Infancy. DiGeorge, A., and Nelson, W. E.: J. Pediat. **38**: 164, 1951.

Three infants with marked generalized atopic eczema which failed to respond to the usual measures of diet elimination and local therapy were treated with ACTH. Within 24 hours after the institution of ACTH therapy, there was dramatic improvement of the rash and subsidence of the itching in each case. Complete clearing of the skin occurred within 3 or 4 days. When the drug was stopped, the rash soon reappeared. A second course was again followed by clearing of the rash, but discontinuance of the drug or reduction of the dose brought on an exacerbation of the lesions. No untoward effects were noted during the short periods of time the drug was used in each case. Because ACTH appears to be effective in producing remissions in generalized atopic eczema for as long as the drug is continued, it can be useful during periods of severe exacerbation when other methods have failed. J. S.

A Standardized Patch Test. Schwartz, L.: Ann. Allergy **8**: 63, 1950.

A standard patch for testing patients with contact dermatitis is suggested. The proposed standard patch consists of a square piece of flannel measuring 3 square centimeters which becomes saturated with 0.2 c.c. of the liquid test material, a square piece of uncoated regenerated cellulose about one inch on each side for insulation, and a piece of elastoplast of a special shape measuring 3 inches across the diagonal. E. W.

The Role of the Antihistaminic Drugs in Producing Cross-Sensitization Dermatitis. Peck, S. M.: New York State J. Med. **50**: 2690, 1950.

Three cases in which sensitivity reactions developed to antihistaminic drugs are reported. In 2 cases, sensitization probably resulted from previous treatment with sulfapyridine. Once the sensitivity developed, reactions were also noted to other antihistaminics previously well tolerated. Reactions to Pyribenzamine and Thephorin in the same patient were difficult to explain on the basis of a common immunochemical group. Another case observed in which the dermatitis occurring after the use of Thephorin ointment was followed by the development of an apparently unrelated paraphenylenediamine sensitivity. The last case reported had a paraphenylenediamine dermatitis and then developed a spontaneous sensitivity to certain antihistaminics. It is suggested that a common secondary allergen may be formed in the body to account for the relationship between the antihistaminics and paraphenylenediamine. B. S.

Skin Eruption Due to Chloramphenicol (Chloromycetin). Usndek, H. E., Curtiss, W. P., and Neill, E. J.: Arch. Dermat. & Syph. **64**: 217, 1951.

A 67-year-old asthmatic woman with bilateral atypical virus pneumonia and mild congestive failure was treated, while in the hospital, with numerous medications including penicillin, digitoxin, pentobarbital, codeine, aureomycin, ephedrine, tripelennamine, diphenhydramine, chloramphenicol, streptomycin, and aminophylline. On the twenty-third day of hospitalization, she developed a generalized erythematous maculopapular eruption. The use of all drugs except Chloromycetin and Pyribenzamine was discontinued, but the rash persisted. Two days later, the administration of chloramphenicol was discontinued and the eruption faded rapidly. When chloramphenicol therapy was resumed, the rash reappeared with greater severity. Withdrawal of the drug was followed by rapid disappearance of the rash. C.

Otorhinology and Ophthalmology

Allergy to Cold in the Respiratory System. Characteristics and Incidence in the Allergic Patient. An Experimental Study. Mathov, E.: Ann. Allergy **8**: 366, 1950.

Forty patients with allergic symptomatology of the respiratory tract, who had remissions of their symptoms, placed their hands and lower forearms in cold water at a temperature of 0° to 3° C. for ten minutes. Nasal smears were taken and examined for eosinophiles before and after these tests were made. Forty per cent of the patients subjected to the experiment stated that they suffered from respiratory symptoms through the action of cold. Only 17 per cent showed symptoms when tested by immersion of hands in cold water and 20 per cent showed a significant rise in their nasal eosinophilic counts following this test. Skin manifestations to cold, such as urticaria, were rarely encountered. Most of the patients who experienced symptoms as the result of exposure to cold were benefited by antihistaminic therapy. The author concludes that the respiratory symptoms resulting from this exposure to cold are due to a truly allergic mechanism and not to a vasomotor reflex. E. W.

Allergy to Cold as an Occupational Disease. Clinical and Experimental Study on 100 Workmen in Meat-Packing Factory. Mathov, E.: Ann. Allergy **8**: 373, 1950.

An investigation was conducted on 100 employees who worked in the freezing chambers of a meat-packing factory at temperatures ranging from –3° to –30° C. These men had been employed in this plant for from 2 to 7 years. Fifty-two per cent stated that they had symptoms on exposure to cold. Objective physical evidence of cold sensitivity was found in 27 per cent after exposure to these temperatures for an hour. In 81.4 per cent of these, there was a positive eosinophilic index (i.e., the difference between the eosinophilic content of the nasal mucus before and after the test). No similar rise was found in any of the others studied. The symptoms of all of the workmen who manifested allergy to cold improved either partially or wholly with antihistaminic drugs. E. W.

A Cyto-Histological Method as a Diagnostic Aid in Allergic Antral Sinusitis. Stromme, O.: Ann. Allergy **8**: 362, 1950.

A method for determining eosinophil counts of antral washings is described. The solid material present in the antral washings was mixed with

four times its volume of 8.7 per cent saccharose in saline to dissolve the mucus. This suspension was centrifuged and the sediment transferred to a pipette tube to which was added serum and Duboin's fixation solution. After this suspension had been centrifuged, the sediment plug was fixed in alcohol, embedded in paraffin, cut in longitudinal sections, and stained for microscopic examination. This method is recommended as a useful diagnostic aid in selected cases. E. W.

Miscellaneous Allergies

Clinical and Pharmacologic Studies With Allylmercaptomethyl Penicillin (Penicillin "O"). Adair, C. V., Woodin, W. G., and Bunn, P. A.: Am. J. Med. **11**: 188, 1951.

Allylmercaptomethyl penicillin (penicillin O) appears to parallel benzyl penicillin (penicillin G) in its speed and degree of absorption after oral and intramuscular administration. Serum and spinal fluid levels, rate and amount of excretion, and clinical and bacteriologic response, were essentially similar to those obtained after administration of penicillin G. Daily doses as high as 12 million units were tolerated without untoward effects.

Twenty-five patients showing hypersensitivity reaction to penicillin G were treated with penicillin O. In the majority of cases with the delayed type of reaction to penicillin G, a change to penicillin O produced a marked decrease or, more often, total disappearance of the allergic phenomenon. Penicillin G could be readministered to the majority of patients after from 2 to 14 days of penicillin O administration without recurrence of the allergic reaction. This does not indicate that penicillin O acts as a desensitizing agent, but merely suggests that the acquired hypersensitiveness to penicillin G is, in most instances, a temporary one, and that, as has been observed clinically, natural desensitization may take place within a few days. Penicillin O rarely produced any reactions in the patients studied and therefore may provide a safer method for administering penicillin to patients with hypersensitiveness to penicillin G.

Untoward reactions to penicillin occur in from 0.5 to 2.7 per cent of patients receiving the antibiotic and fall into 3 groups: (1) local reactions after instillation of penicillin or after local contact; (2) the "id" phenomenon; and (3) the delayed or acute anaphylactoid reaction. The latter is by far the most common and is of most concern in the treatment of patients with acute infections. It is generally considered to be due to hypersensitivity to a salt of benzyl penicillin or to its in vivo protein-bound material. This type of reaction can be controlled by the substitution of penicillin O for G. The "id" and contact reactions do not respond favorably to the administration of penicillin O.

Skin and patch testing with penicillin O or G do not aid in predicting the success to be expected by substituting O for G in individuals suffering from hypersensitivity reaction, nor are they practicable in confirming the presence of hypersensitiveness. F.

Allergy to Penicillin O and the Management of Penicillin Sensitivity. Siegal, S.: Am. J. Med. **11**: 196, 1951.

Five patients with hypersensitivity reactions to penicillin G were shown by skin test to possess cross sensitivity to penicillin O. These results refute the claim that penicillin O can be safely administered to patients suffering from hypersensitivity reactions to penicillin G. F.

Allergy to Pituitary Corticotrophic Hormone. Feinberg, S. M., Feinberg, A. R., Bigg, E.: J. A. M. A. **147**: 40, 1951.

A 60-year-old woman who had been receiving cortisone for the treatment of rheumatoid arthritis was placed on ACTH therapy. The first injection of 25 mg. was followed within 5 minutes by alarming symptoms consisting of generalized urticaria, angioneurotic edema involving the larynx, asthma, and profound shock. Recovery ensued following emergency therapy. Subsequent questioning revealed that the patient had received a previous course of ACTH about one year prior to the present incident. During the first series of ACTH injections, she developed urticaria after the initial dose. With subsequent injections, the urticaria became progressively worse; the twelfth dose was followed by angioneurotic edema and shock.

Skin tests made with corticotrophin derived from pork, sheep, and beef produced whealing reactions in dilutions as high as 1:10,000,000. Tests made with 1:1000 dilutions of beef, pork, and sheep muscle extract were entirely negative. Other pituitary preparations and pituitrin, such as antuitrin, all produced positive skin reactions. A sheep corticotrophin peptide also produced definite positive skin reactions. Positive passive transfer reactions were obtained with porcine corticotrophin, but could not be elicited with the other corticotrophic hormones or with the pituitary compounds which had given positive direct skin reactions. F.

The Presence of Complement-Fixing Antibodies Against Brain Tissue in Sera of Persons Who Had Received Antirabies Vaccine Treatment. Koprowski, H., and LeBell, I.: Am. J. Hyg. **51**: 292, 1950.

A relatively high incidence of neurologic complications follows the administration of antirabies vaccine. On the suspicion that individuals who have had a previous course of this vaccine and that allergic persons might experience more severe reactions to such treatment, quantitative studies of complement-fixing antibodies for rabbit and human brain tissue were carried out in 50 human subjects before and at several intervals after the administration of antirabies vaccine. Of 16 patients who received a 7-day course of treatment, none developed brain antibodies. Of 34 who received a 14-day course, 50 per cent acquired complement-fixing antibodies for both human and rabbit brain at some time after the vaccination. The highest titers were observed between the 14th and 56th days after vaccination and in one case were still detectable at 227 days. The titer was generally lower for human brain tissue than for rabbit brain. In 6 cases with high levels of antibodies, no ill effects were observed during the several months observation period. Six individuals of a total of 3,305 treated with antirabies vaccine developed neuroparalysis and 3 of the 6 were studied for antibodies. Two were found to have very high titers of antibrain antibodies and the third case, from whom blood was first drawn relatively late in the course of illness, showed a rather low titer. In contrast, no complement-fixing antibodies were found in either of 2 cases of multiple sclerosis. It was concluded that further studies are necessary to establish whether the incidence of neuroparalytic accidents is greater in proportion to the length of antirabies treatment. K.

Antigenicity of Sarcomata Undergoing Atrophy in Rats. Lewis, M. R., Aptekman, P. M.: J. Immunol. **67**: 193, 1951.

Sarcomata originating in the host's own species were implanted into rats and were permitted to grow for several days. The blood vessels supplying the tumors were then ligated and the growth allowed to remain in situ for an

additional 2 to 4 days. Normal rats were inoculated with extracts prepared from the atrophied tumors and were reinoculated a few weeks later with viable sarcomata tissue. The animals treated with atrophied tumor extracts showed a remarkable immunity. Those rats receiving tissue which had atrophied for 3 or 4 days demonstrated 100 per cent immunity. It is suggested that the atrophying tumor tissues are antigenic and capable of producing immunity when transplanted into susceptible rats. R. W.

Therapeutic Effect of an Allergic Reaction to Food on Rheumatoid Arthritis. Polymenakos, L. G.: Lancet **1**: 831, 1951.

A 68-year-old man, who was undergoing an acute attack of rheumatoid arthritis, suddenly developed angioedema and urticaria following the ingestion of fish. During the next few weeks, the patient's condition showed dramatic improvement, which began about 15 hours after the onset of the allergic reaction. The author suggests that the allergic reaction caused enough stimulation of the pituitary adrenal axis to produce a remission in the arthritis. R. W.

Migraine Headache: An Analysis of 124 Cases Treated by Head Traction Manipulation and Thiamin Chloride. Braaf, M. M.: New York State J. Med. **51**: 528, 1951.

Eighty-eight cases of typical migraine and 36 cases of atypical migraine were studied. A familial history of headache was present in 48 per cent of the typical cases and in 11 per cent of the atypical ones. Allergy was a definite factor in 36 per cent of the classical forms and in 6 per cent of the atypical types. Marked psychoneurotic tendencies were found in 2 per cent of the typical cases and in 11 per cent of the atypical forms. Trauma to the cervical spine, either direct or indirect, was considered one of the most important factors in the causation of migraine. A history of such trauma was obtained in 42 per cent of the typical migraine cases and in 56 per cent of the atypical ones. Thirty-nine per cent of the classic cases and 78 per cent of the atypical forms showed a loss of the lordotic curve on x-ray examination of the cervical spine. In all cases, definite localized tenderness was found upon digital pressure of the upper cervical spine on the same side as the headache. Therapy consisted of head traction, manipulation of the neck and intramuscular injection of 200 mg. of thiamin chloride at least three times a week for a period of 1 or 2 months. From 75 to 100 per cent improvement was obtained in 75 per cent of the cases. The less chronic the condition and the younger the patient at the time of onset of therapy, the better were the results. Patients with a history of migraine attacks due to specific foods could tolerate those foods after therapy, suggesting that the "apparent food 'allergy' was secondary probably to vagal irritation induced reflexly by stimulation of the upper cervical nerves." B. S.

Anaphylaxis

Protection by Flavonoids Against Histamine Shock. Wilson, R. H., Booth, A. N., and DeEds, F.: Proc. Soc. Exper. Biol. & Med. **76**: 540, 1951.

Rutin, quercitrin, quercetin, or methyl hesperidin chalcone was injected intraperitoneally into guinea pigs. Thirty minutes later, they were shocked with histamine via the intravenous route. The LD_{50} dose of histamine varied with the batch of animals, so that each group of guinea pigs had to be standardized separately. Changing the dose of histamine by 5 per cent was sufficient to change an LD_{50} to an LD_0 or to an LD_{100}. All 4 flavonoids afforded slight protection against histamine shock. The discrepancy in results of experiments of this type reported in the literature may be due to the use of inadequately standardized animals or excessive histamine dosage. B. S.

Pharmacology, Physiology, and Pathology

Studies on the Mechanism of the Shwartzman Phenomenon. Certain Factors Involved in the Production of the Local Hemorrhagic Necrosis. Stetson, C. A., Jr.: J. Exper. Med. **93**: 489, 1951.

When normal rabbits were given intravenous injections of Shwartzman-preparatory agents (meningococcal toxin, somatic antigen of Shigella paradysenteriae, rabbit liver glycogen, or agar), a profound leukopenia was noted within a few minutes and became fully developed within an hour. Ovalbumin produced a similar effect when injected into an egg-sensitized rabbit but did not show this activity when injected into a normal animal. Thrombocytopenia developed soon after the injection of glycogen or meningococcal toxin. Histologic examination of the lung tissue of three rabbits, injected wtih meningococcal toxin or glycogen intravenously and sacrificed within 10, 30, and 60 minutes, revealed rough correlation between the degree of leukopenia in the circulatory blood and the number of leukocytes in the lung capillaries where the polymorphonuclear leukocytes rapidly accumulated. Masses of platelets were also found in these vessels. Human or rabbit heparinized blood plasma mixed with glycogen or agar and examined under a vaseline-sealed cover slip exhibited clumping of platelets with these clumps coalescing and encompassing the polymorphonuclear leukocytes. These masses became visible macroscopically and readily adhered to test tube walls and dust or lint particles. The clumping was reversible after a period of time, which correlated with the amount of glycogen added, and the released polymorphonuclear leukocytes resumed their normal motility. Citrated or oxylated blood samples failed to show the above phenomenon unless calcium was subsequently added. Bacterial toxins did not elicit this effect in vitro and it is suggested that they may initiate in vivo a chain of events which results in the production of a clumping factor. This hypothesis would be consistent with the fact that a longer time is required to produce a Shwartzman phenomenon with such toxins (2 to 4 hours) than with glycogen or agar (15 to 30 minutes).

Meningococcal toxin was injected intracutaneouly in 8 rabbits. After 18 hours, 2 animals were sacrificed and the remainder were injected intravenously with meningococcal toxin and sacrificed in pairs at 15 minutes, 2 hours, and 4 hours thereafter. Histologic examination revealed no change in uninjected normal skin. At the prepared areas, however, prior to intravenous injection, the capillaries and smaller veins were thrombosed and necrosis of vessel walls and neighboring tissue was evident. There was perivascular cuffing of the majority of the small skin veins by polymorphonuclear leukocytes which were also adherent to the intimal surfaces of these vessels. Capillaries, arterioles, and arteries appeared normal. Fifteen minutes after the intravenous challenge the lumen of the veins and capillaries in the prepared sites were obliterated by plugs of platelets and polymorphonuclear leukocytes. At 2 hours, the plugs persisted and there was evidence of necrosis of the leukocytes in the exudate surrounding the veins and in the thrombi. The vein walls were becoming necrotic. At 4 hours, when hemorrhage could be seen grossly, there was marked arteriolar and capillary dilatation and hemorrhage from the small veins which still contained a remnant of the thrombus.

Attempts to produce hemorrhage in Brown-Pearce rabbit carcinomas by the injection of glycogen failed. However, in mice with "sarcoma 180" the intravenous injection of rabbit liver glycogen or meningococcal toxin intravenously produced extensive hemorrhage in the tumor within 1 to 2 hours. Tumors removed as soon as 20 minutes after such an injection showed thrombi of platelets and leukocytes in the veins and small capillaries. It is suggested that the increased susceptibility of the blood vessels in prepared skin may be due to the large amounts of lactic acid produced in these areas, which favors

the adherence of leukocyte-platelet thrombi. The occurrence of cellular thrombi in tumors may be related to the high lactic acid formation in these tissues. K.

Neural Mechanisms Involved in Itch, "Itchy Skin," and Tickle Sensations. Graham, G. T., Goodell, H., and Wolff, H. G.: J. Clin. Investigation **30**: 37, 1951.

Itching was produced in normal adults using cowhage, an "itch powder," applied to approximately 1 sq. cm. of skin. Within a few minutes, the skin for several centimeters proximally and distally around the itching area became hypoalgesic to pin prick and around this zone was an area of hyperalgesia, approximately 0.5 cm. wide. Intense itching could not be distinguished from pain. When a cutaneous nerve on the forearm was blocked by local anesthesia so as to leave the initial "fast" or prickling pain sensation to pin prick without abolishing the slower diffuse burning pain response, cowhage elicited itching without burning. When pain was abolished completely, itching was not felt. When the upper arm was compressed with a sphygmomanometer cuff set at 200 mm. Hg for 20 minutes, pin prick and cowhage applied to the hands elicited a pain and itch, respectively, each with a burning sensation following a prolonged latent period. "It is suggested that 'prickling' itch is carried by the myelinated fibers responsible for 'first' pain, and that 'burning' itch is carried by the unmyelinated fibers responsible for 'second' pain." Using thermal radiation technique, it was found that pain threshold was lowered in the itching area. In surrounding areas of skin, pain threshold was constant or slightly elevated when a central area was itching. It is likely that itching stimuli activate pain endings in the skin but not to a sufficient degree to cause pain. Thus, less heat need be added to produce pain. Itch occurs when pain receptors are weakly stimulated.

Pin pricks several times in the zone of itching or on surrounding skin abolished itching for several minutes, although the pain from pricking faded in from 10 to 15 seconds. Pin prick at a distance but in the same dermatome as the itch also abolished itching. Painful electrical stimulation of a cutaneous nerve for 2 minutes produced a zone of hyperalgesic skin surrounding the area. Cowhage applied to this area evoked either no response or pain, but not itching. When the nerve was partially anesthetized so as to abolish the hyperalgesia, cowhage then elicited itching. It is suggested that the sensation of itch results from the presence in the spinal cord of impulses traveling in circuits of internuncial neurons, with a consequent patterned discharge up to the spinothalamic tracts. Pain or scratching in the same dermatome breaks up the internuncial circuit and thus gives relief.

Itchy skin and tickle differ from itch only in that awareness of movement is included and, like itch, are mediated by the nerve fibers which transmit pain. K.

The Effect of Epinephrine on the Pulmonary Circulation in Man. Witham, A. C., and Fleming, J. W.: J. Clin. Investigation **30**: 707, 1951.

The effects on the pulmonary circulation of levo-rotatory epinephrine administered intravenously and intramuscularly in doses of from 0.5 to 0.7 c.c. of a 1:1000 solution were studied in 13 patients by means of an intracardiac catheter placed in the pulmonary artery, dye dilution techniques for blood flow and volume, and a high frequency recording manometer for peripheral arterial pressure.

The mean pulmonary artery pressure rose in every case following the intramuscular injection of epinephrine. The systolic component increased an

average of 6 mm. Hg and the diastolic rise averaged 2 mm. These values returned to normal within 20 minutes in all except 3 patients who evidenced a more prolonged effect. Pulmonary "capillary" pressure measured in 5 cases rose slightly or not at all. Pulse rate increased, cardiac index increased, and heart stroke volume increased following epinephrine. Circulation of dye from pulmonary to femoral artery occurred more rapidly. The pulmonary blood volume index decreased slightly but not significantly and appeared to be related to the change in cardiac index. "When cardiac output increase is substantial, as in most of our cases, the dilated areas can be served without calling on the pulmonary circulation, but when the peripheral action of the drug is the more pronounced, there is relatively little change in output, and the pulmonary vascular circuit is drained to supply the dilated peripheral arterial beds." Evidence is presented which indicates that epinephrine causes a decrease in the cross-sectional areas of the pulmonary terminal arterioles without affecting capillary or venous pressures. K.

Acute Glomerulonephritis Following Administration of Rhus Toxin: Report of a Fatal and a Near Fatal Case. Shaffer, B., Burgoon, C. F., and Gosman, J. H.: J. A. M. A. **146**: 1570, 1951.

Two cases of acute glomerulonephritis, one fatal in outcome, which occurred one week and four weeks, respectively, after therapeutic injections of Rhus toxin, are reported. The active principle in Rhus toxin is apparently a toxic oil with three active components, one of which, urushiol, is a catechol compound. Simple chemicals of this type may induce both epidermal and general sensitivity by acting as hapten allergens. That the acute glomerulonephritis occurring in each of the reported cases was due to such sensitization is suggested by the fact that there was a latent period between the last injection of Rhus toxin and the first sign of kidney disease. In the fatal case, eosinophilia, urticaria, and histologic changes in the kidney suggested that death was the result of an allergic phenomenon. The Council of Pharmacy and Chemistry of the American Medical Association has warned of the potential dangers and of the questionable value of these extracts. F.

Inhibition of Red Cells Isoagglutination by Allergenic Extracts—Preliminary Report. Binaghi, R. A.: Ann. Allergy **8**: 354, 1950.

Extracts of a number of inhalants possessed the property of inhibiting red cell isoagglutination. The agglutinating titer of the sera was diminished from 2 to 16 times. A close correlation between the inhibitory property and the biologic activity was found, although the biologic test was more sensitive. The use of this test was an in vitro method of estimating the potency of allergenic extracts is suggested. Pollen extracts were not used in these experiments. E. W.

Experimental Hypersensitivity in the Rabbit. Blood and Tissue Concentrations of Foreign Proteins Labelled With Radioactive Iodine and Injected Intravenously. Latta, H.: J. Immunol. **66**: 635, 1951.

Bovine serum gamma globulin and human serum albumin were each labelled with radioactive iodine (I^{131}) and injected intravenously into rabbits. The blood levels, urine excretions, and tissue concentrations were determined at intervals up to 14 days. The results showed that bovine serum gamma globulin usually disappeared from the blood within 9 days, whereas iodinated human albumin persisted in some animals for as long as 2 weeks. On the

whole, iodinated protein and unlabelled proteins were shown to have very similar disappearance rates from the blood. The concentration in any one tissue at a given time was roughly proportional to the blood concentration, but the lymph nodes appeared to concentrate the foreign protein, especially in the medulla, out of proportion to their blood content. R. W.

A Method for the Demonstration of Tissue Antibody. Hayes, S. P., Dougherty, T. F., and Gebhardt, L. P.: Proc. Soc. Exper. Biol. & Med. **76**: 460, 1951.

Small pieces of subcutaneous tissue were removed from immunized mice, spread thinly on glass slides and air-dried. A ring of petroleum was then placed around the tissue, homologous antigen was added, and the preparation sealed with a sterile coverslip. Organs to be examined were cut with a sharp scalpel and imprints, made by touching the cut surface directly to a glass slide, were treated in the same manner as the subcutaneous tissue. After the addition of antigen, the preparations were incubated and read in 1 or 2 hours and again after overnight incubation. When agglutinating antibodies against bacteria or sheep erythrocytes were present, well-defined bacterial or erythrocytic aggregates were seen adhering tightly to the surface of lymphocytes. When these antigens were used for sensitization of mice and rabbits, agglutinating antibody was found in specimens of the loose connective tissue from the site of injection before it appeared in the blood. Antibody was not found in the liver or spleens of the immunized animals before it began to circulate. These findings support the hypothesis that antibodies can be formed locally and that lymphocytes contain specific homologous antibodies. B. S.

Effect of Histamine and Antihistaminics on Coagulation of Normal and Heparinized Rabbit Plasma. Haley, T. J., and Stolarsky, F.: Proc. Soc. Exper. Biol. & Med. **76**: 299, 1951.

Using normal and heparinized rabbit plasma, histamine and the antihistaminic drugs (with the exception of Thenfadil, Methapyrilene, and Thonzylamine) were found capable of inactivating heparin in vitro. At concentrations below a critical level, the drugs had little or no effect upon the coagulation system. The critical levels necessary for an antiheparin effect would be toxic levels insofar as human dosage is concerned. It is postulated that the antiheparin activity of these compounds may be due to the chemical combination of the basic antihistaminic molecule and the acidic heparin molecule. B. S.

Poliomyelitis: Precipitation by Injections. Goerke, L. S.: California & West. Med. **74**: 383, 1951.

The slightly higher incidence of paralysis among children recently vaccinated or immunized over that in children who were not is considered to be statistically not significant.

The incidence of paralysis in 1948 in a group of 27 children with polio under the age of 12 who were immunized or vaccinated was 77.8 per cent. Among 843 polio cases during that year in a similar age group, the paralysis incidence was 74.3 per cent. Among the total of 1,321 cases for 1948, 30 cases had their onset within 34 days after an injection of some kind. This figure included 18 cases with onset within 10 days after an injection. In only 8 of the 30 cases could the paralysis be related to the limb which had been the site of the injection.

The author concludes: "It appears inadvisable to permit the possible chance occurrence of poliomyelitis following injections to interfere with the continued mass elimination of diseases equally crippling and fatal." H.

The Effect of ACTH in Acquired Hemolytic Anemia. Unger, L. J.: Am. J. Clin. Path. **21**: 456, 1951.

A 56-year-old woman with acquired hemolytic anemia was found to have auto-antibodies for red cells so that she could not be transfused. The administration of ACTH 100 mg. per day for 8 days, followed by 60 mg. for 13 days, resulted in clinical improvement, a rise in her red blood count, disappearance of jaundice, and a fall in red cell antibody titer from 4 units to 2 units. She was then able to tolerate a transfusion of washed red cells without reaction. The dosage of ACTH was tapered off, but after its discontinuance she suffered a drop in red cell count and a rise in her icterus index. K.

Epinephrine in the Treatment of Migraine. Sperber, P. A.: Ann. Allergy **8**: 126, 1950.

Eight patients with severe migraine were treated with small doses of epinephrine. In 6 of these, this drug was considered more satisfactory than ergotamine for relief of the headache. E. W.

Bacterial Production and Destruction of Histamine in Vitro. Alin, K.: Acta Allergologica **3**: 136, 1950.

The capacity of bacteria to form and destroy histamine is influenced by the pH. A capacity to decarboxylate histidine to histamine in an acid medium was found in all investigated strains of *E. coli* and Salmonella. Some Salmonella strains could also produce histamine in a neutral medium. No strains of *P. aeruginosa* were found to form histamine. The ability to destroy histamine was demonstrated in both *P. aeruginosa* and *E. coli.* An acid medium during bacterial growth stimulates the formation of decarboxylase and inhibits the formation of histaminase in bacteria. H.

Effect of Cortisone on Acute Streptococcal Infections and Post-Streptococcal Complications. Hahn, E. O., Houser, H. B., Rammelkamp, C. H., Jr., Denny, F. W., and Wannamaker, L. W.: J. Clin. Investigation **30**: 274, 1951.

During an epidemic of streptococcal tonsillitis and pharyngitis, 87 acutely ill patients were treated with cortisone over a 5- or 6-day period. Eighty-seven similarly affected patients were employed as controls and were given saline injections. The only other medication used was codeine for severe headache. Serological studies and cultures were made weekly for 5 weeks and electrocardiograms were taken soon after the acute symptoms had subsided. The infecting organism was group A beta-hemolytic streptococcus. Cortisone had little or no effect on chills, headache, malaise, or time of disappearance of physical signs. Persistence of sore throat and fever was greater in the treated group. Suppurative complications occurred during cortisone administration in 1 treated patient and in 3 controls. Typical rheumatic fever developed in 2 treated and in 5 control cases. Prolonged PR intervals on electrocardiograms taken 21 days after onset of illness were noted in 5 treated cases (1 with rheumatic fever symptoms) and in 4 controls (3 with symptoms of rheumatic fever). Cortisone-treated cases showed a more persistent blood leukocytosis. Antistreptolysin titers increased slightly less in the treated cases in the first week, while cortisone was being administered, but the treated group had slightly higher titers after 2, 3, and 4 weeks. K.

Multiple Testing by Electrophoresis. Morse, C. O.: Ann. Allergy **8**: 331, 1950.

An apparatus for multiple testing by the electrophoretic method is described. The active electrode consists of a flexible rubber sponge pad one-half inch thick in which are embedded small rubber sockets. These sockets are connected in series by fine flexible wires. Plastic caps are screwed in the sockets by means of a metallic stud which forms the base of the cup. A cotton ball which is saturated with the extract to be used in the test is placed into each cup. This active electrode is connected with a galvanic apparatus receiving its current from two 45 volt B batteries. The indifferent electrode is a sheet of zinc wrapped in a towel and connected to the positive pole. In this manner, as many as 60 tests can be performed simultaneously using 0.05 milliampere for each cup in use. In spite of large numbers of pollen extracts applied simultaneously and the occurrence of many strongly positive reactions, constitutional reactions have never been observed. The author states that this method is of value in testing small children. E. W.

A Study of Reactions Following Administration of Crude and Purified Diphtheria Toxoid in an Adult Population. Pappenheimer, A. M., Jr., Edsall, G., Lawrence, H. S., and Banton, H. J.: Am. J. Hyg. **52**: 353, 1950.

Of 2,712 Army personnel Schick-tested, 40 per cent were found to be positive. The percentage of positives decreased with age, 50 per cent of those under 20 years old and 36 per cent of those over 35 years of age being positive. Five diphtheria toxoid preparations of varying degrees of purity were administered in 5 Lf doses, subcutaneously, to various groups of men. Of 54 severe systemic reactions encountered, all but one occurred in the Schick-negative group; of 95 severe local reactions, 87 occurred in patients who were Schick-negative before immunization. Severe reactions in the Schick-positive group occurred only in those with skin reactions to the Schick "control" test, which was designed to point out toxoid reactors and consisted of 0.008 Lf of crude toxoid (equivalent to 10 times the dose of Schick toxin) instead of the usual heated toxin. There were significantly fewer severe reactions in subjects under 20 years of age given purified toxoid than occurred in those receiving crude toxoid. In men over 30 years of age, reactions tended to be more frequent and severe than in younger men regardless of purity of material. Purity of preparation diminished the incidence of reactions in those having a positive cutaneous response to the Schick "control" test. K.

The Antigenicity of Single, Graded Doses of Purified Diphtheria Toxoid in Man. Edsall, G., Banton, H. J., and Wheeler, R. E.: Am. J. Hyg. **53**: 283, 1951.

A marked decrease in Schick-negative adults has been noted within the last 10 years. Diphtheria antitoxin titers were measured in 167 medical students 51 per cent of whom were found to have below 0.004 units of antitoxin per ml. of blood, the threshold of immunity as correlated with the Schick test. The subjects were then divided into subgroups and given saline or purified diphtheria toxoid subcutaneously in doses ranging from 1.0 to 0.0016 Lf. The volume of the injection was kept constant at 1.0 ml. Three or 4 weeks later, antitoxin titers were again determined; in 87 students, titers were also obtained 5 months later from two- to fivefold changes, either an increase or decrease, was observed in several control subjects. The average gain in titer was roughly proportionate to the square root of the increase in the amount of antigen administered. A number of subjects with initial titers below 0.001

unit per ml. failed to show a rise in titer after inoculation. In 26 of 30 subjects with initial titers greater than 0.001 but less than 0.01 unit per ml., the final titers rose to more than 0.01 unit per ml. regardless of the dose administered. Subjects with very high initial (over 0.1 unit) titers, however, did not show so marked an increase. Recheck of students 5 months after immunization again showed the superiority of the 1.0 Lf dose, although there was a noticeable drop from the very high 3-week titer. It is concluded that "in a population known to have previously acquired immunity, a satisfactory immunity level may be maintained by subcutaneous periodic administration of relatively small doses of toxoid." Two severe reactions in the group of 29 subjects receiving the 1.0 Lf dose suggested that this dose is close to the upper limit of tolerance in an unselected population. K.

Impotence: An Unusual Side Reaction in Antihistaminic Therapy. Jeannes, S. W.: Ann. Allergy **8**: 407, 1950.

Sexual impotence was observed in 2 men following antihistaminic therapy. In both cases, Pyribenzamine was the drug which caused these unusual side reactions. In neither case, did Benadryl produce this effect. Theophorin caused a similar side reaction in one of the cases. Virility returned in each patient when the use of the offending drug was discontinued. E. W.

Adrenocortical Activity and Immunity. Bjorneboe, M.: Nord. med. **45**: 383, 1951.

The writer reviews the experimental studies relating to the effect of cortisone and ACTH on the concentration of circulating antibodies. The author has proposed a theory to explain the beneficial effect of adrenocortical hormones in human diseases. In diseases where antibody formation is injurious, substances inhibiting antibody formation (adrenocortical hormones) will be effective. In infectious diseases in which the clinical course indicates that a favorable prognosis depends on the ability of the organism to form antibodies, adrenocortical hormones will not be effective. H.

Toxic Reactions to Meralluride Injection (Mercuhydrin Sodium Solution). Reeves, G. A.: J. A. M. A. **146**: 1594, 1951.

A 53-year-old man, suffering from hypertensive cardiovascular disease with failure, was given daily intramuscular injections of mercuhydrin. After the eleventh and twelfth injections, the patient complained of retrosternal pain and had an elevation in temperature. After the thirteenth injection, there was intense burning of the palms and subungual regions. Generalized aching in the back, thighs, and legs was followed by a shaking chill, a rise in temperature to 103.8° F., cyanosis, and apprehension. Urinalysis showed one-plus albumin and from 1 to 3 hyaline casts per field. Treatment with mercuhydrin was discontinued. Subsequently, the patient was treated for another attack of pulmonary congestion and peripheral edema with mercaptomerin sodium without untoward reaction. F.